

Preventing Dementia and Enhancing Brain Health

Henry Brodaty





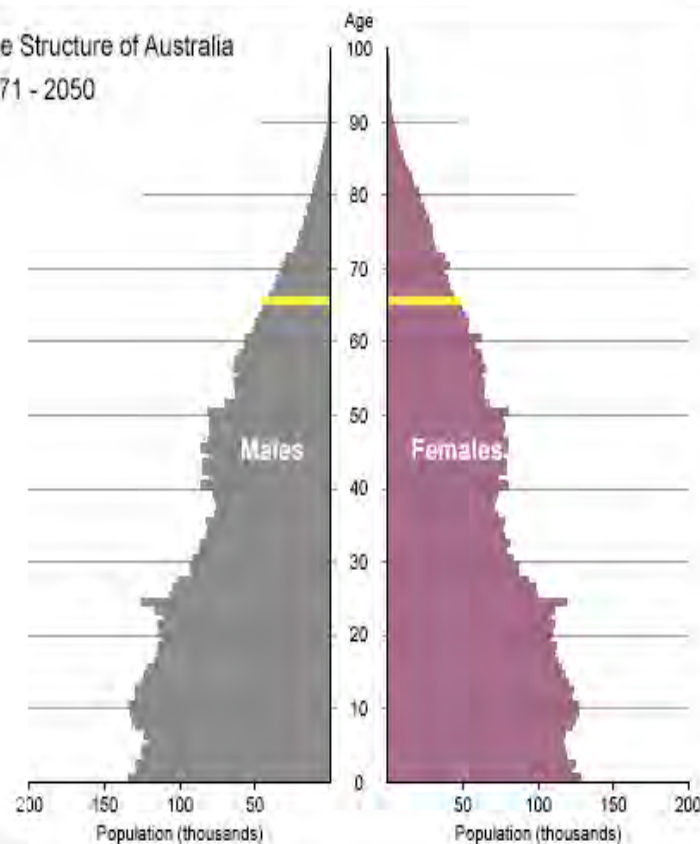
Ronald and Nancy Reagan, USA



"I have recently been told that I am one of the Americans who will be afflicted with Alzheimer's disease. ... I will continue to share life's journey with my beloved Nancy and my family. I plan to enjoy the great outdoors and stay in touch with my friends and supporters"



Age Structure of Australia
1971 - 2050



1971

Total (mil.): 13.1

Aged 65

Born 1905-1906

Males: 44187

Females: 47704

Sex Ratio: 92.6
(males per 100 females)

☐ Highlight surplus of
males or females

Animate

speed

Start: 1971

1980

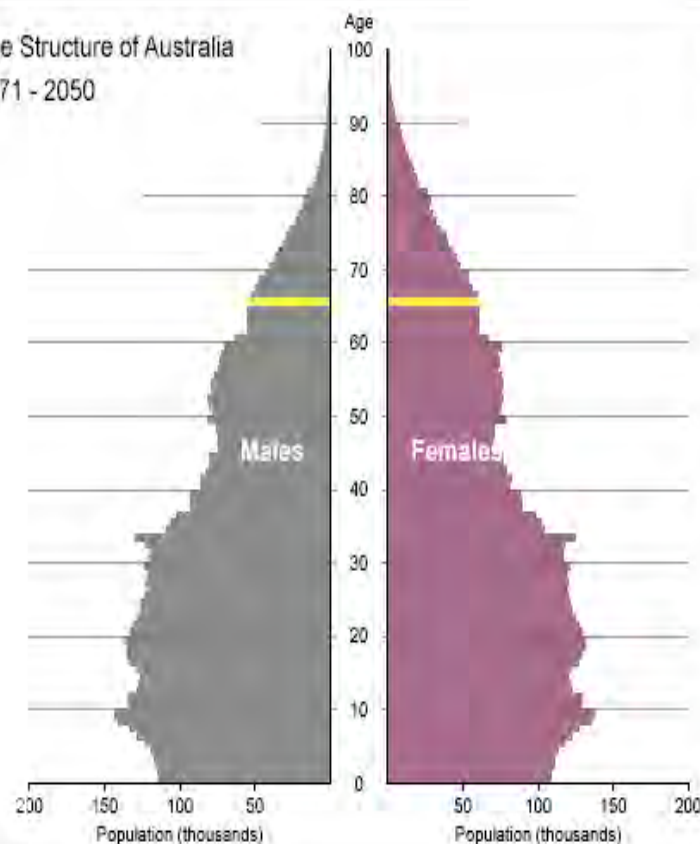
2000

2020

2040

End: 2050

Age Structure of Australia
1971 - 2050



1980

Total (mil.): 14.7

Aged 65

Born 1914-1915

Males: 54014

Females: 59940

Sex Ratio: 90.1
(males per 100 females)

☐ Highlight surplus of
males or females

Animate

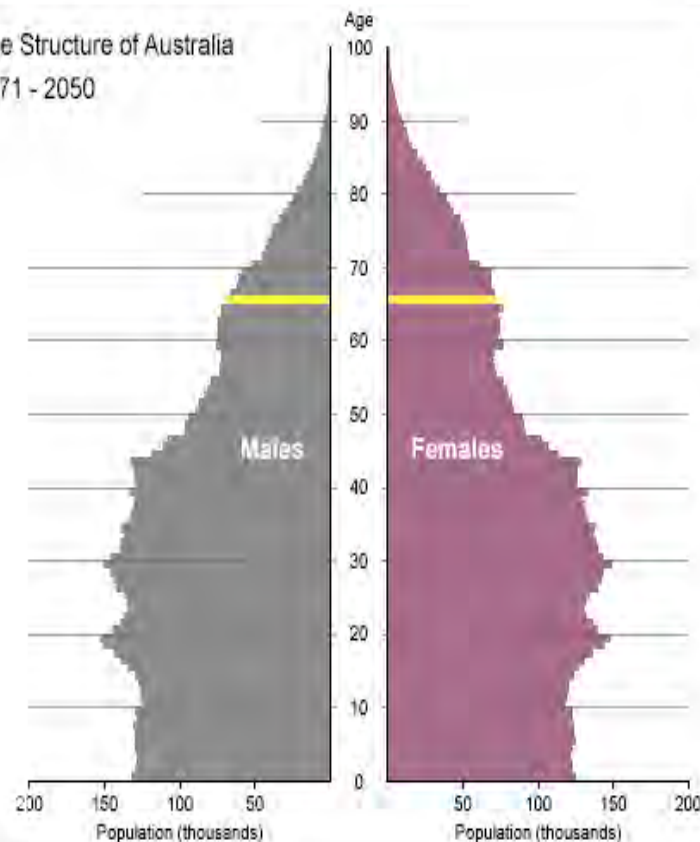
speed

Start: 1971



End: 2050 [Help](#)

Age Structure of Australia
1971 - 2050



1990

Total (mil.): 17.1

Aged 65

Born 1924-1925

Males: 86937

Females: 71442

Sex Ratio: 93.7
(males per 100 females)

☐ Highlight surplus of
males or females

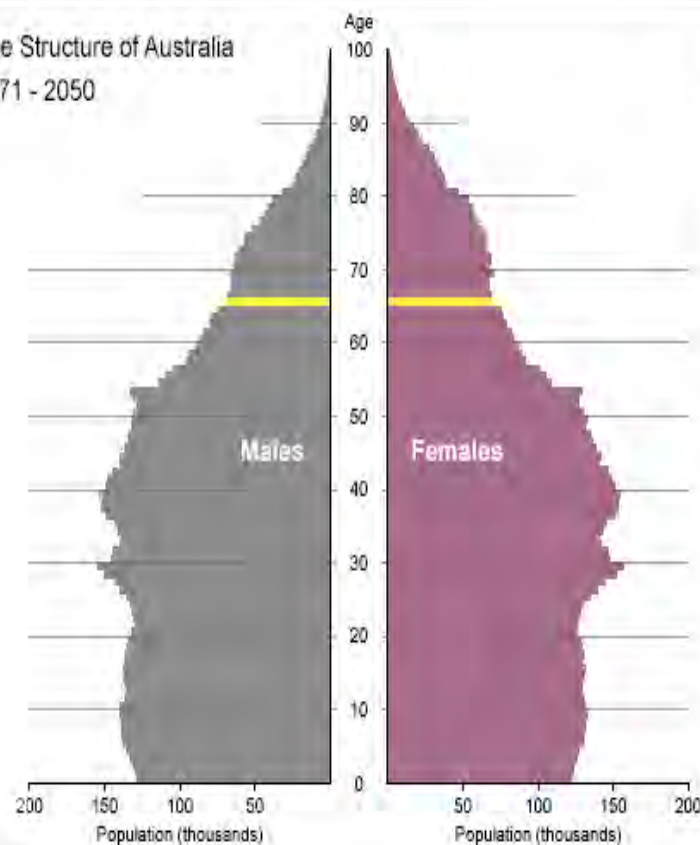
Animate

speed

Start: 1971 End: 2050 [Help](#)

1980 2000 2020 2040

Age Structure of Australia
1971 - 2050



2000

Total (mil.): 19.2

Aged 65

Born 1934-1935

Males: 68162

Females: 70380

Sex Ratio: 96.8
(males per 100 females)

☐ Highlight surplus of
males or females

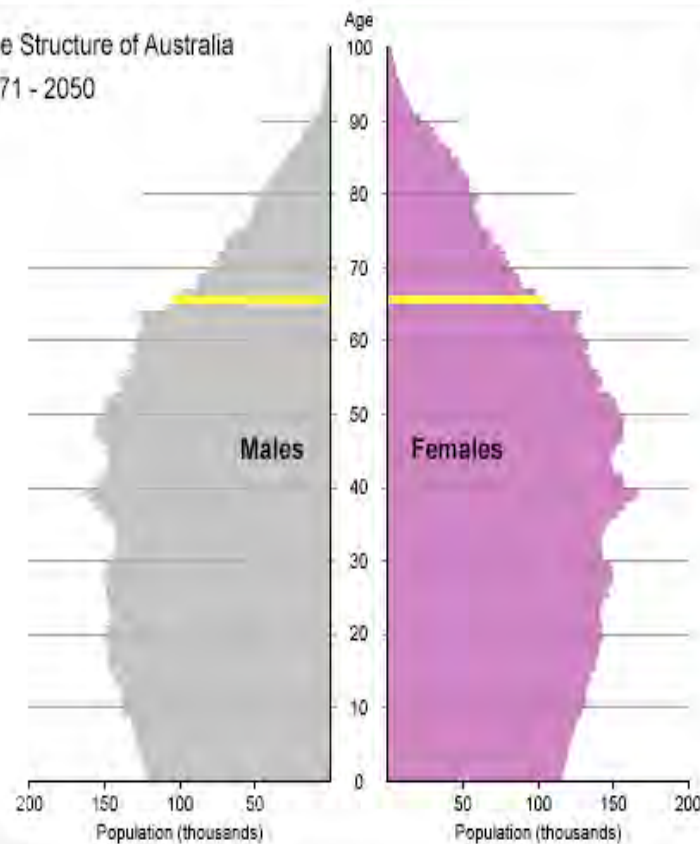
Animate

speed

Start: 1971 End: 2050

1980 2000 2020 2040

Age Structure of Australia 1971 - 2050



2010

Total (mil.): 21.3

^a Projected Data

Aged 65

Born 1944-1945

Males: 103626

Females: 103321

Sex Ratio: 100.3
(males per 100 females)

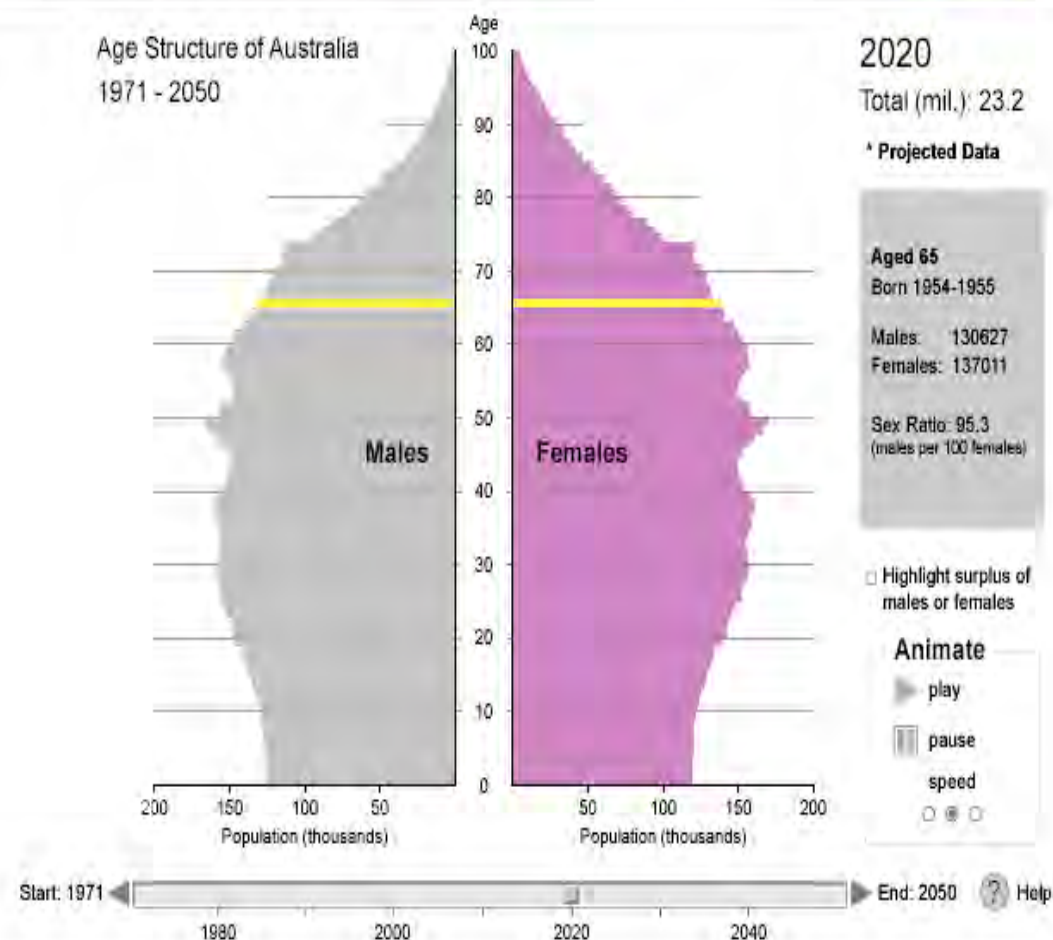
☐ Highlight surplus of
males or females

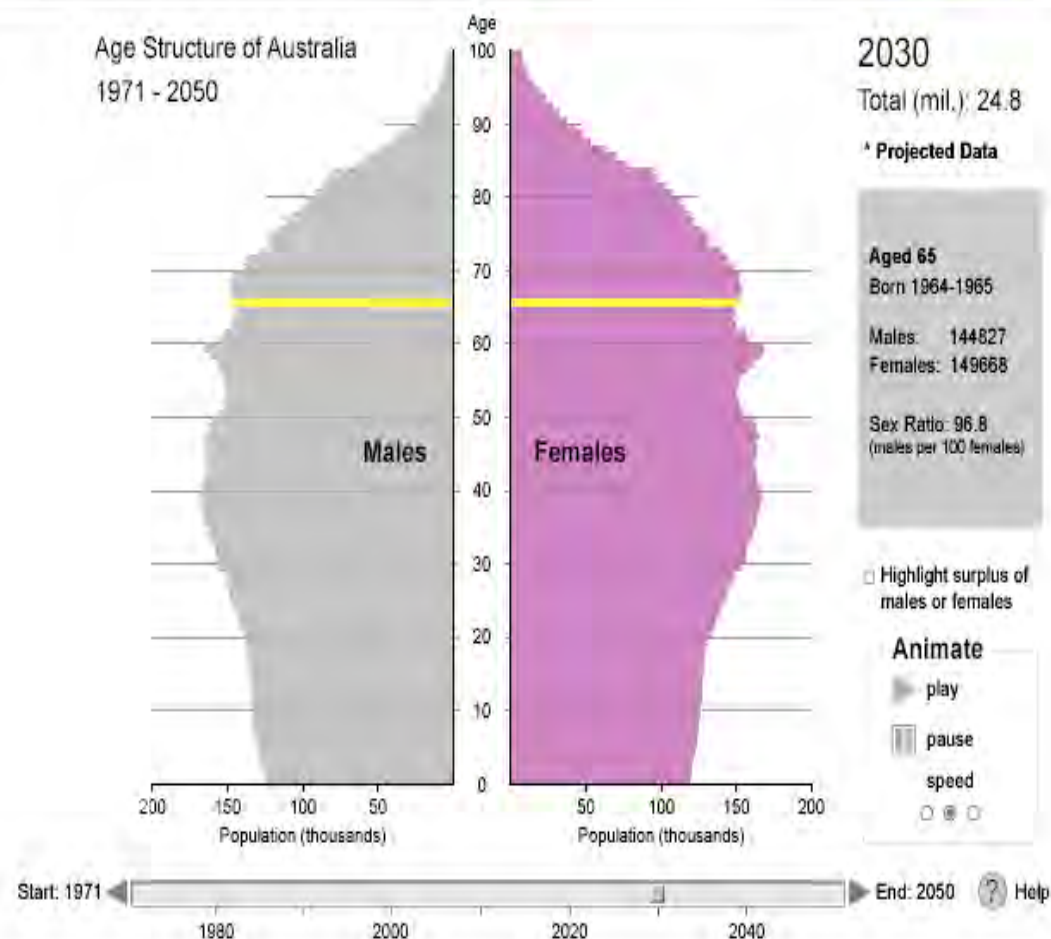
Animate

speed

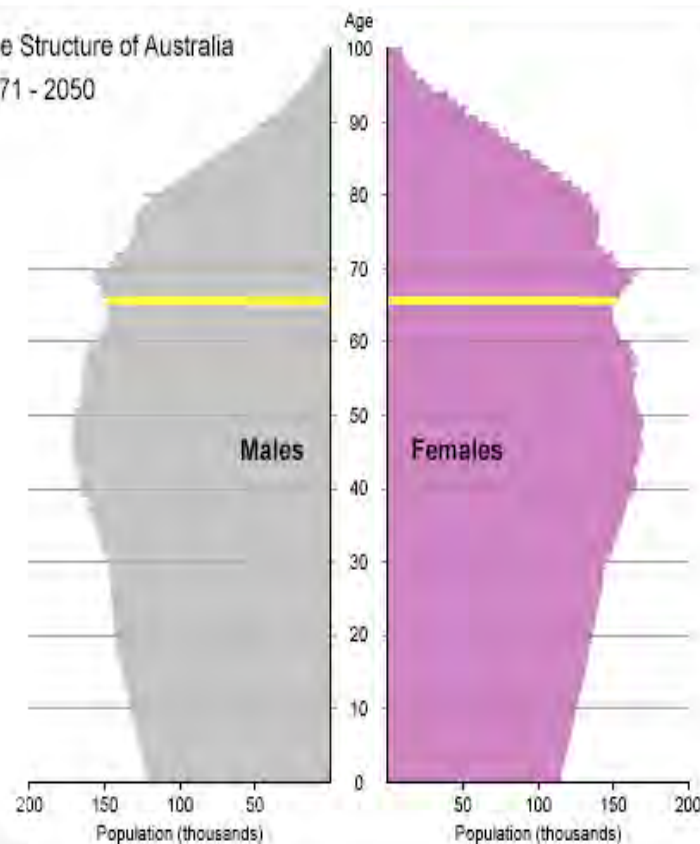
Start: 1971 End: 2050

1980 2000 2020 2040





Age Structure of Australia
1971 - 2050



2040

Total (mil.): 25.8

^a Projected Data

Aged 65

Born 1974-1975

Males: 147773

Females: 151127

Sex Ratio: 97.8
(males per 100 females)

☐ Highlight surplus of
males or females

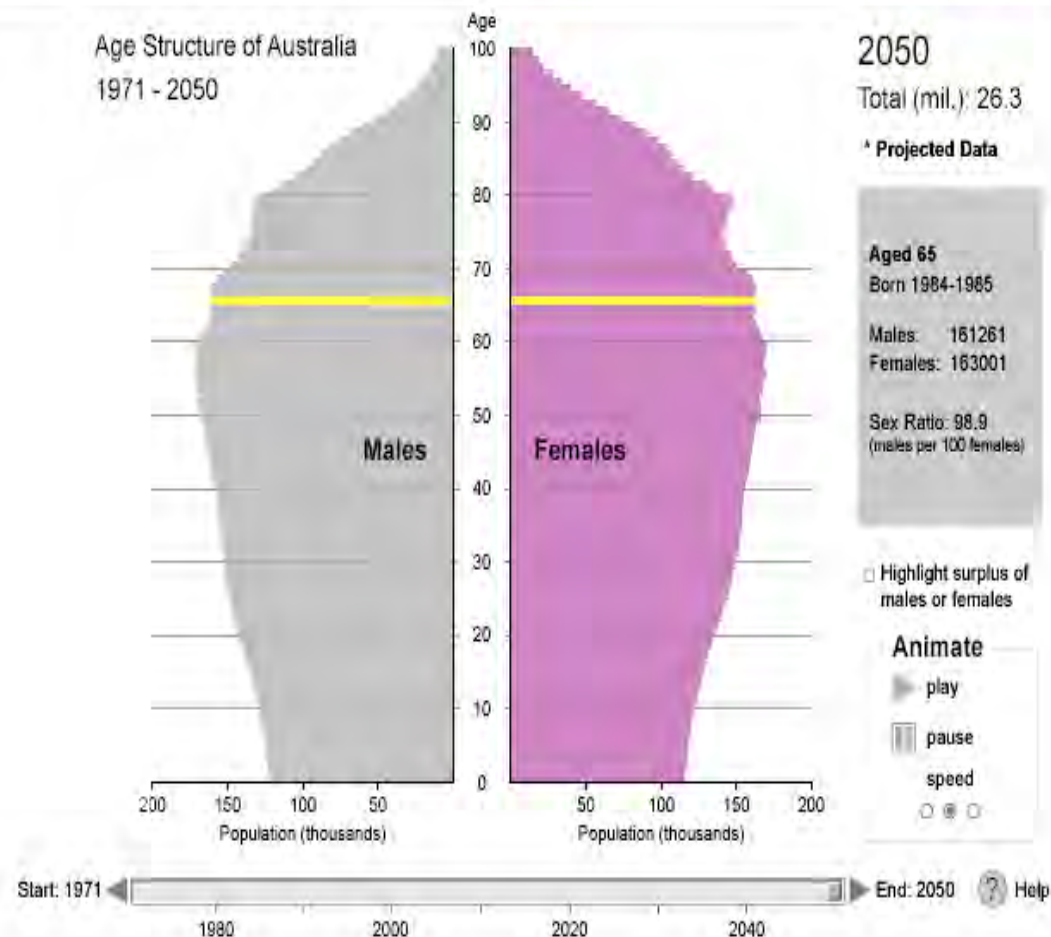
Animate

speed

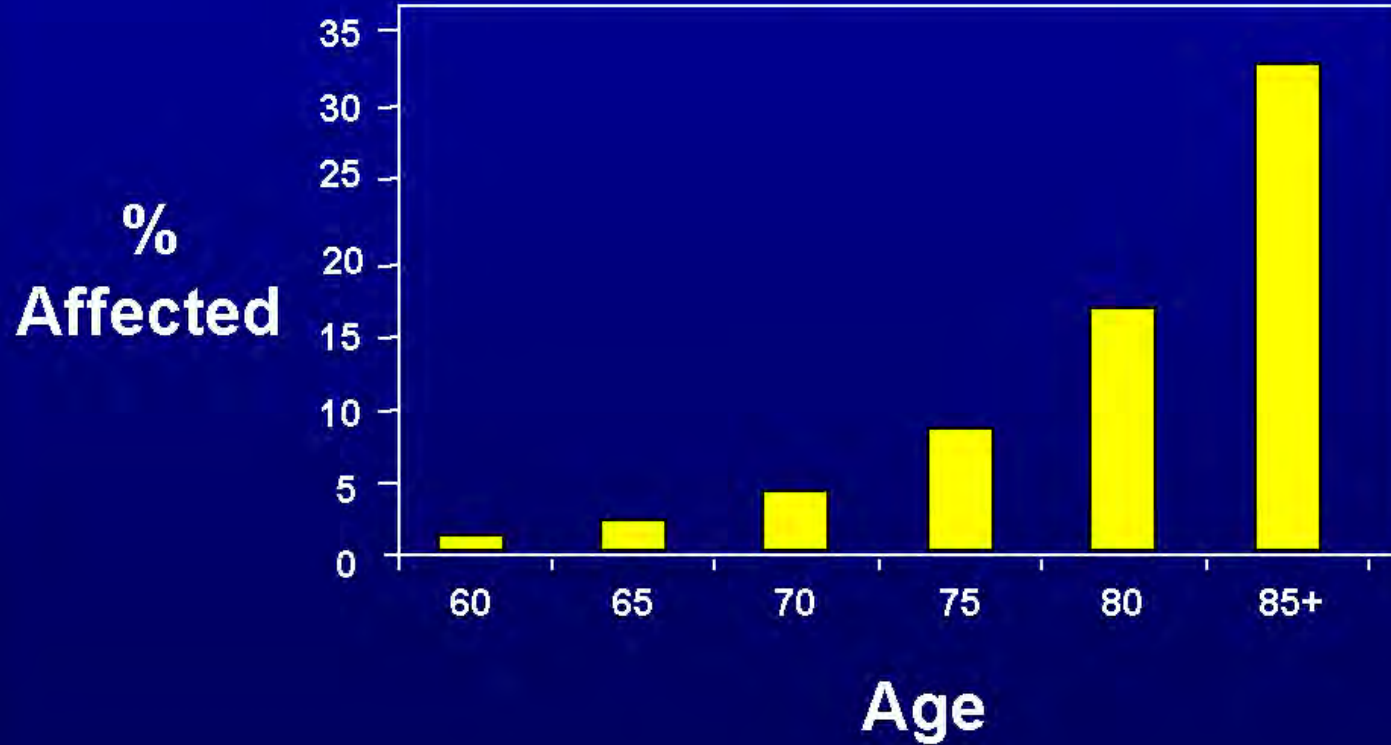
Start: 1971



End: 2050



Dementia Doubles in Frequency Every 5 Years After Age 60



Evans et al. *JAMA*. 1989.
Jorm et al. *Acta Psychiatr Scand*. 1987.

Can we prevent dementia?

- The adult brain weighs about 1.3 kg
- Dementia shrinks it to 1/2 its usual size



What are we aiming to prevent: dementia, Alzheimer's disease, vascular dementia, mixed dementia?

- **With ↑age, % of pure type of dementia decreases**
- **In older people, mixed dementia is more common than Alzheimer's disease**
- **80%+ of older people with dementia have cerebrovascular disease at post mortem**
- **Most effort has been on preventing/delaying Alzheimer's disease**
- **Vascular disease of the brain, strokes may be more preventable**

Elimination vs Postponement

- **Disease elimination**
 - eg smallpox vaccination
 - best prospect is AD vaccine
- **Disease postponement¹: delay AD onset by...**
 - 2 years, ↓ prevalence by 20%
 - 5 years, ↓ prevalence by 50%

¹Brookmeyer et al. (1998)

Life Course Approach: childhood

- Genetic determinants
 - Environmental determinants
 - Foetal maldevelopment
 - Low birth weight *for gestational age*
 - Low education
 - Low parental education & occupation
 - Low socio-economic status
 - Dietary history
 - Loss of parent before 11yo
- Reduced cognitive reserve

Is early life the most important target?

- 70% of world dementia in developing countries where there are high rates of:
 - Low foetal birth weight for gestational age
 - Poor education
 - Poor socio-economic environment

YOUR BRAIN MATTERS

A GUIDE TO HEALTHY HEARTS & MINDS

- Look after your heart
- Be physically active
- Mentally challenge your brain
- Follow a healthy diet
- Enjoy social activity

yourbrainmatters.org.au

Cardiovascular Factors



**The human heart
Leonardo Da Vinci**

Blood Pressure & Dementia



- Mid-life hypertension associated with late-life dementia
- Treating blood pressure decreases risk in some studies
- Each year of treatment decreases risk

Caveats

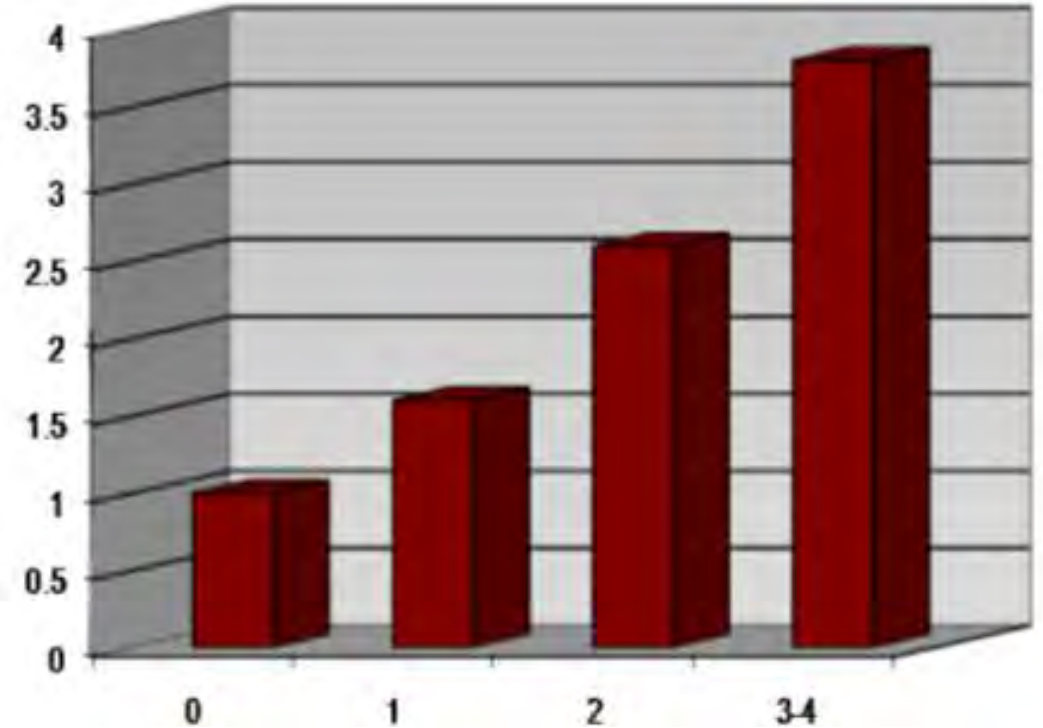
- Can harm if lower BP too much in older old

Dosage Effect

The more vascular risk factors
the greater AD/ dementia risk

- *Hypertension*
- *Smoking*
- *Hypercholesterolemia*
- *Obesity*
- *Diabetes*
- *Physical inactivity*

Luchsinger et al 2005



Number of risk factors

Slide adapted from Michael Valenzuela

SPRINT- MIND Trial

- Does treating high blood pressure to target < 120 mm Hg systolic better than < 140 mm
- 9361 hypertensive older adults with high CV risk but no diabetes, dementia or stroke
- At 1 year, mean sBP 121 vs 134
- Less mild cognitive impairment in intensive BP treated group and trend for less dementia
- Also less increase over 4 years in white matter lesions

Statins to prevent AD



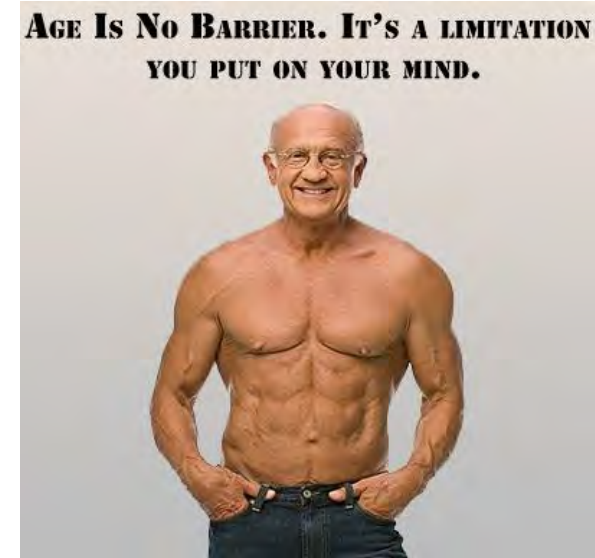
- Statins neither prevent nor increase risk of cognitive impairment or dementia¹
- Benefits of statins may vary by type of statin, sex, race²

¹ McGuinness B et al, 2016; CD003160 (1)
Cochrane Database of Systematic
Reviews

² Zissimopoulos J et al, JAMA Dec 2016

Physical activity = Protective

- Several studies show physical activity protective against cognitive decline, dementia, Alzheimer's, vascular dementia
 - More is better – puffed, weights
 - At least three times per week
 - At least 150 minutes per week
- Check with your doctor



¹Jedrzejewski et al (2007). Alz Dem; 3:98-108; ² Lautenschlager et al (2008) JAMA; 300(9):1027-1037;

³Ravaglia et al (2007) Neurology; ⁴Larson et al (2006) Ann Intern Med; 144:73-81; ⁵Laurin et al, Arch Neurol 2001;58:498-504; ⁶Middelton et al, PLoS ONE 2008;3(9):e3124

Can aerobic exercise protect against dementia?

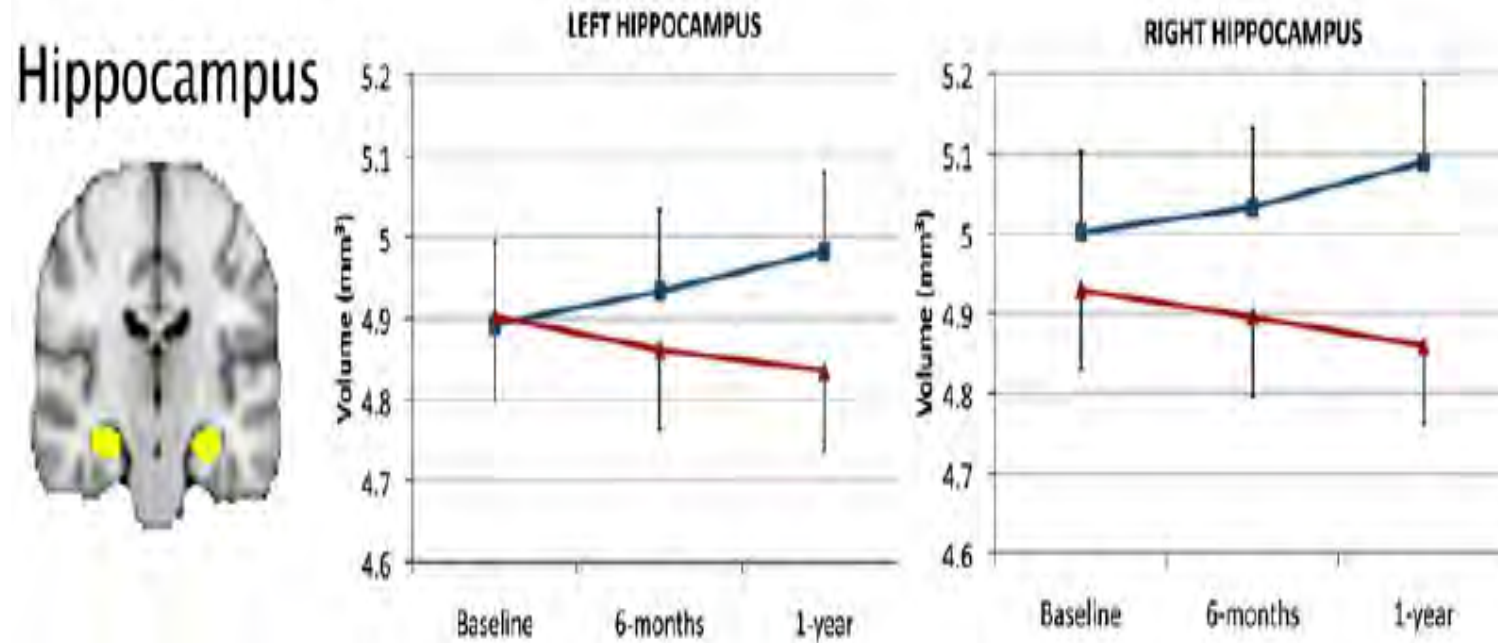
- Preserves cognition and slows cognitive decline
- Decreased incident dementia
- 8/11 Randomised Control Trials in healthy older persons: cognition & fitness improved
- Biomarkers improved, e.g. brain volume
- Animal studies – growth factors improved, brain derived neurotrophic factor improved, more new nerve cells, less inflammation
- Less Alzheimer's disease pathology

Physical activity

- Physical activity benefits older adults to prevent dementia: Never too late to start; never too early
- Moderate intensity (brisk walking) 30 min 5d/wk
- Evidence for specific exercise not clear; more than one type and more exercise may be better
- Resistance training better in SMART Trial²
- Combine physical, social and mental activity better?
 - Eg dancing

Denkinger et al. *Z Gerontol Geriatr* 2012; 45:11–16 DOI 10.1007/s00391-011-0262-6
Fiatarone Singh MA et al *JAMDA* 2014;15:873-80

The power of physical activity



Erickson et al., 2011

Physical activity benefits

- Improved fitness
- Improved physical health - ↓ heart disease, Hi BP, diabetes, some types of cancer, osteoporosis, sarcopenia
- Reduced morbidity & mortality
- Improved mental health
- Improved confidence, quality of life

Cognitive interventions healthy older adults and people with Mild Cognitive Impairment

- **20 RCTs with healthy adults**
 - Memory improvements in 17/20
- **6 RCTs with MCI**
 - Memory improvements in 4/6
- **Unclear whether these improvements generalise to everyday activities**
- **Review of cog. training or rehabilitation in dementia**
 - 11 RCTs, no benefit

Obesity in Mid-Life



Mid-Life Obesity

- Compared to normal weight, midlife obesity increases risk of dementia later in life
 - BMI 25-30: 34% increased risk
 - BMI > 30: 91% increased risk
- Obesity paradox: In late life being overweight is not a risk factor, may be protective



Mind your diet

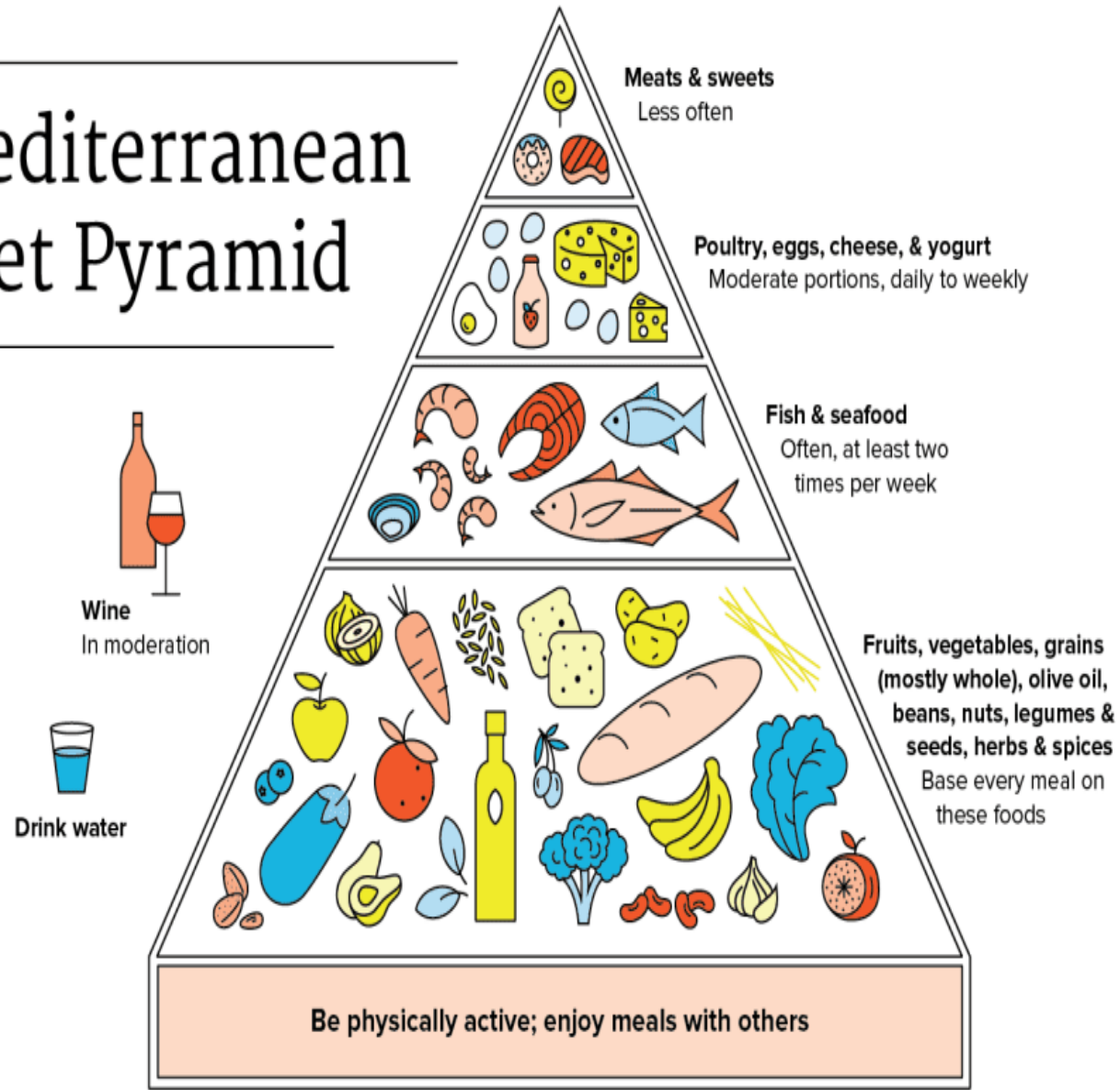
- Mediterranean diet
- Antioxidants

What is Mediterranean diet?

- Abundant plant foods
- Fresh fruit as typical daily dessert
- Olive oil as principal source of fat
- Dairy products (cheese, yogurt)
- Fish and poultry - low to moderate
- 0- 4 eggs week
- Red meat - low amounts
- Wine - low to moderate amounts
- Total fat = 25% to 35% of calories
- Saturated fat $\leq$ 8% of calories



Mediterranean Diet Pyramid



Western diet v Eastern diet



Centenarian Hotspots Blue Zones



Blue Zone: Okinawa, Japan



- General female life expectancy = 87yrs
- Increase in centenarians:
 - 30 (1975) → ↑ 1000 (2016)
- ~35% function independently
- Factors influencing longevity:
 - Diet?
 - Genetics?
 - Physical activity?

Willcox et al. (2016), Mechanisms of Ageing & Development

Okinawa: Reasons for Longevity

- **A lean diet with fewer calories:**
 - **Vegetables**
 - **Tofu**
 - **Miso soup**
 - **A little fish or meat**
- **Confucian-inspired adage:**
 - **"hara hachi bu" = until your stomach is 80% full**

Nutrition / Supplements



- Fish✓ ω3 ?
- Vitamin D ?
- Caffeine ?
- Vitamin E ?
- Vitamin C x

Food sources better than supplements

B Vits and homocysteine

- **OPTIMA: Folate 0.8mg + Vit B₁₂ 0.5mg + B₆ 20mg**
 - Reduce brain atrophy and improve cognition
 - Mainly in people with high homocysteine
- **Two systematic reviews and one trial no benefit from homocysteine lowering Rx**

- Smith AD et al, PLoS ONE, 2010; Douaud et al. PNAS 2013;110:9523-28
- Ford AH, Almeida OP Systematic review 19 RCTs *J Alz Dis.* 2012;29:133-49 doi: 10.3233/JAD-2012-111739
- Clarke R et al Am J Clin Nutr 2014;100:657–66
- van der Zwaluw, Neurology;2014;83:1–9

Vit D, NSAIDs, fish, curcumin

- **Vit D – low levels of Vit D are common and associated with development of dementia**
 - **No evidence that taking Vit D lowers risk**
- **Anti-inflammatories – mixed epidem. evidence**
- **Fish oil – some evidence, natural source ie fish (epidemiological)**
- **Curcumin – some evidence (laboratory)**

Smoking and AD

- **Current smoking**
 - increase risk for AD
- **Previous smoking**
 - Risk not significantly increased

Alcohol

- **Weak evidence benefit of moderate alcohol**
 - i.e. abstinent → higher risk, j-shaped curve
- **What is *moderate*?**
- **Not all studies confirm**
- **Heavy alcohol is risk factor**
- **Which alcohol – (red) wine?**
 - Evidence not strong
- **Alcohol linked to higher rates of cancer**

Natural therapies

- Ginkgo biloba X
- Turmeric, curcumin ?
- DHA, omega 3 ??
- Fo-ti root
- Soy isoflavone
- Vitamin E, Selenium X
- Saffron
- Brahmi
- Huperzine A

Ginkgo
leaves



Member of
ginger
family

Unproven but popular on net

- Coconut oil
- Grain Brain
- Ketogenic diet
- Many others??

Promising?

- Resveratrol, activates sirtuins
- Next generation anti-ageing compounds

Hearing loss



Hearing loss and incident dementia

- Lin 2011 RR 2.32 (1.32-4.07)
- Gallacher 2012 RR 2.67 (1.38-5.17)
- Deal 2016 RR 1.55 (1.10-2.19)
- Peripheral hearing loss associated with significant risk for dementia
- Follow-ups 9,12 and 17 years

Social isolation



Socialisation and dementia

- **Less frequent social contact, less social participation, and more feelings of loneliness associated with increased risk of dementia**
- **57% increase risk = comparable to late-life depression 85% and physical 82% incr^d risk**
- **Good social engagement, pooled reduction in risk 22%, (but significant publication bias)**

Penninkilampi R, Casey A-N, Fiatarone-Singh M, Brodaty H. 2018

Hormone Replacement Therapy

- **HRT – neither harmful or beneficial close to menopause**
- **Increased risk in women taking HRT from age 65yr?**



Sleep and dementia



Sleep and dementia

- About 1-in-2 older adults have regular insomnia
- About 1-in-2 older adults have sleep-disordered breathing
- Slow wave sleep associated with amyloid- β protein clearance from brain in animal and human studies
- Sleep-disordered breathing associated with poor sleep
- Poor sleep associated with worse cognition
- Can correcting insomnia and sleep-disordered breathing prevent or delay?
- Does incipient dementia cause sleep disorders?

Environmental factors

- 30% of population attributable risk of AD cases from 7 environmental factors
- If 25% lower prevalence of these risk factors → 3 million fewer AD cases worldwide
- Highest estimated Population Attributable Risk for AD
 - Global: low education contributes $\approx 20\%$
 - USA, Europe, UK : physical inactivity contributes $\approx 20\%$

Barnes & Yaffe, 2011; Norton et al, 2014

How much AD can be attributed to environmental factors?

- 2% diabetes mellitus (type 2)
- **2% midlife obesity***
- 5% midlife hypertension
- 10% depression
- **13% physical inactivity***
- 14% smoking
- **19% cognitive inactivity/education#**

Is incidence of dementia/ cognitive impairment declining?

- Review 14 studies ... trends in dementia prevalence (9 studies) and incidence (5)
- Sweden, Spain, UK, Netherlands, France, USA, Japan and Nigeria.
- All (except Japan) → stable or declining prevalence and incidence of dementia
- Some effects in males; others females only
- No single risk or protective factor fully explains observed trends, but

Is incidence of dementia/ cognitive impairment declining?

-major societal changes and improvements in
 - living conditions, early childhood
 - education
 - healthcare , cardiovascular
- might have favourably influenced physical, mental and cognitive health throughout life, and
- be responsible for ↓ risk of dementia in later life

But.... How reliable are these findings?

- **Most studies are observational or single interventions**
- **Reverse causality?**
 - **Alzheimer's disease builds up in brain over 20+ years before it becomes clinically evident**
 - **Could incipient dementia lead to less cognitive activity, exercise, socialisation, etc**
- **Can intervention studies prove that adopting these recommendations decrease cognitive decline?**

Multi-component intervention studies

- **FINGER**
- **Pre-DIVA**
- **MAPT**
- **HATICE**
- **Maintain Your Brain**

FINGER study

- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability
- Interventions
 - Diet
 - Cognitive training
 - Exercise – PMR and aerobic
 - Manage metabolic & vascular risk factors
 - Social activities

Ngandu et al. *The Lancet*. 2015;
[http://dx.doi.org/10.1016/S0140-6736\(15\)60461-5](http://dx.doi.org/10.1016/S0140-6736(15)60461-5)

FINGER study

- At 2 years improvement on
 - Composite Neuropsychological battery
 - Speed of information processing
 - Executive functioning
 - Complex memory (but not memory overall)
- At 5 years other benefits on health

Ngandu et al. *The Lancet*. 2015;
[http://dx.doi.org/10.1016/S0140-6736\(15\)60461-5](http://dx.doi.org/10.1016/S0140-6736(15)60461-5)

PreDIVA trial

- Long-term, nurse-led vascular care in an unselected population of community dwelling older people is safe and may reduce incidence of non-Alzheimer's dementia
- Potentially clinically meaningful effects in lowering incident dementia in people with untreated hypertension adherent to intervention
- Control treatment was good

Moll van Charante EP, Lancet 2016

Internet-based therapies: Advantages

- Home-based
- Geographically isolated individuals
- Scalable
- Relatively cheap (but not free)

Current trials:

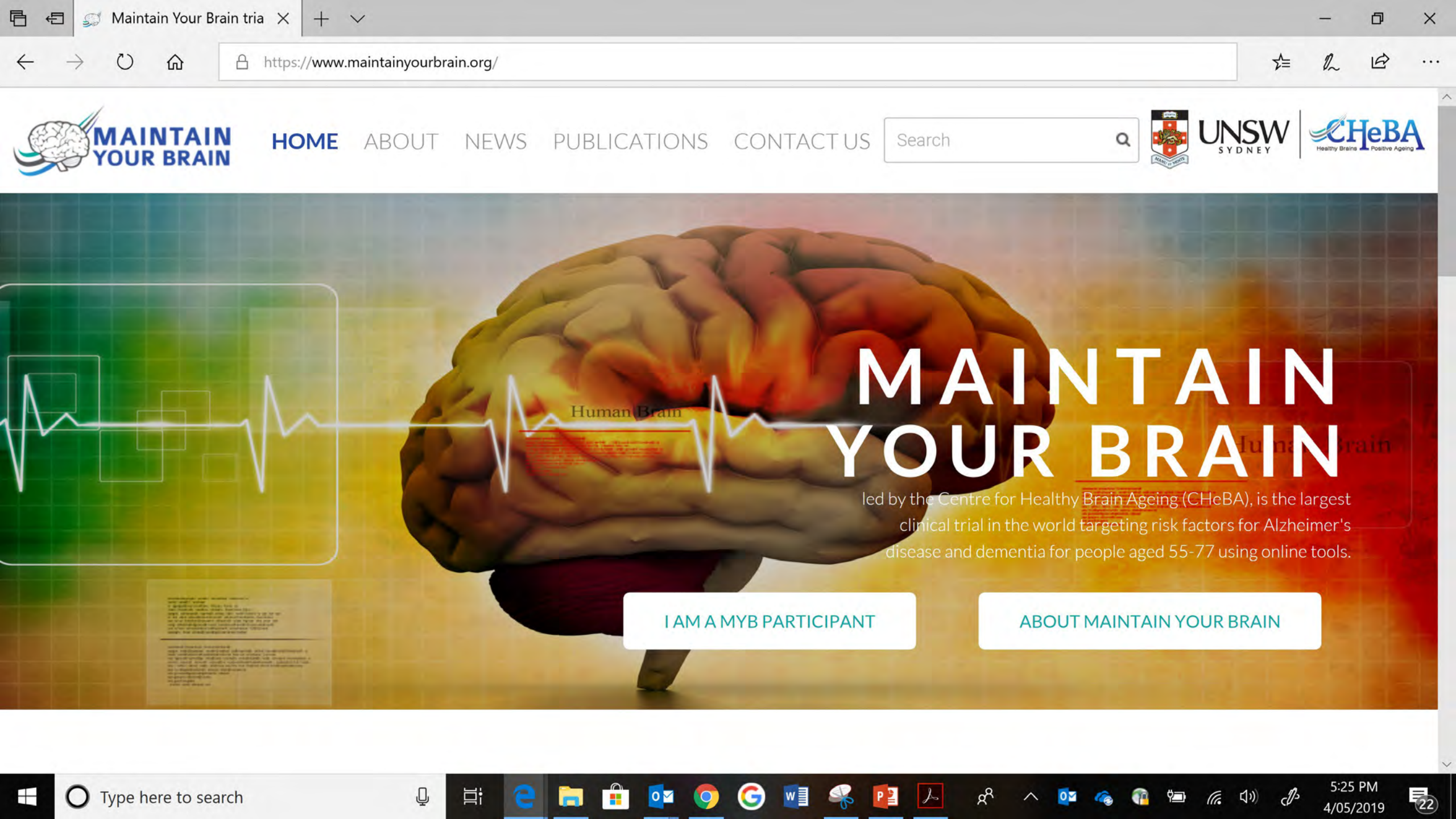
- HATICE (Richard E_BMJ Open 2016;6(6):e010806)
- MYB (Heffernan M et al, 2019)

Internet-based therapies: Disadvantages

- Requires IT Platform development ++
- Requires Central HQ to run and monitor
- Not everyone has computer or internet access or is tech-savvy
- Not yet proven to work

Healthy aging through internet counselling in the elderly (HATICE)

- Develop an innovative, interactive internet intervention platform to optimise treatment of cardiovascular disease in the elderly
- Test this new intervention in a RCT to investigate whether new cardiovascular disease and cognitive decline can be prevented
- Trial completed, not yet published
- Richard E, <http://www.hatice.eu/>



MAINTAIN YOUR BRAIN

led by the Centre for Healthy Brain Ageing (CHeBA), is the largest clinical trial in the world targeting risk factors for Alzheimer's disease and dementia for people aged 55-77 using online tools.

I AM A MYB PARTICIPANT

ABOUT MAINTAIN YOUR BRAIN

RCT: Four basic modules



Physical activity



Diet & nutrition



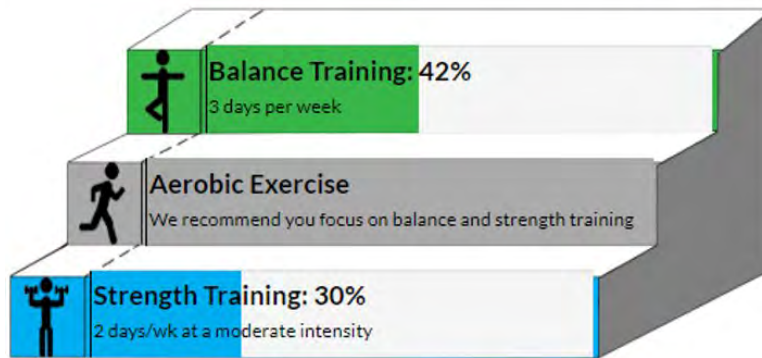
Brain training



Depression

Physical Activity

Welcome to the Physical Activity Module



My Current Activity Level


My Physical Activity Goals


My Feedback History



Strength Training

Your goal for this week is: **Increase the number of exercises you are doing to 4 upper and 4 lower body exercises that you can perform safely, so that you are achieving 45 minutes of strength training per session.** You can find out more information about Strength Training below.


Strength Training
Information and Factsheets


Strength Training Video and
Exercise Cards

Nutrition

Welcome to the Nutrition Module



How to piece it together

The Mediterranean pyramid

The Mediterranean cuisine and lifestyle

The Mediterranean pantry and shopping list

Sample menu plan

Meal and snack ideas

Recipe library

Food allergies, intolerances and drug interactions

Scientific literature

My Mediterranean Goals

The Mediterranean Diet



The Ideal Mediterranean Diet

Brain Training (BTS)

 **Current Exercise: Solitaria**

Exercise 1 out of 17 for this session


HOPE JUICE
Memo Pair

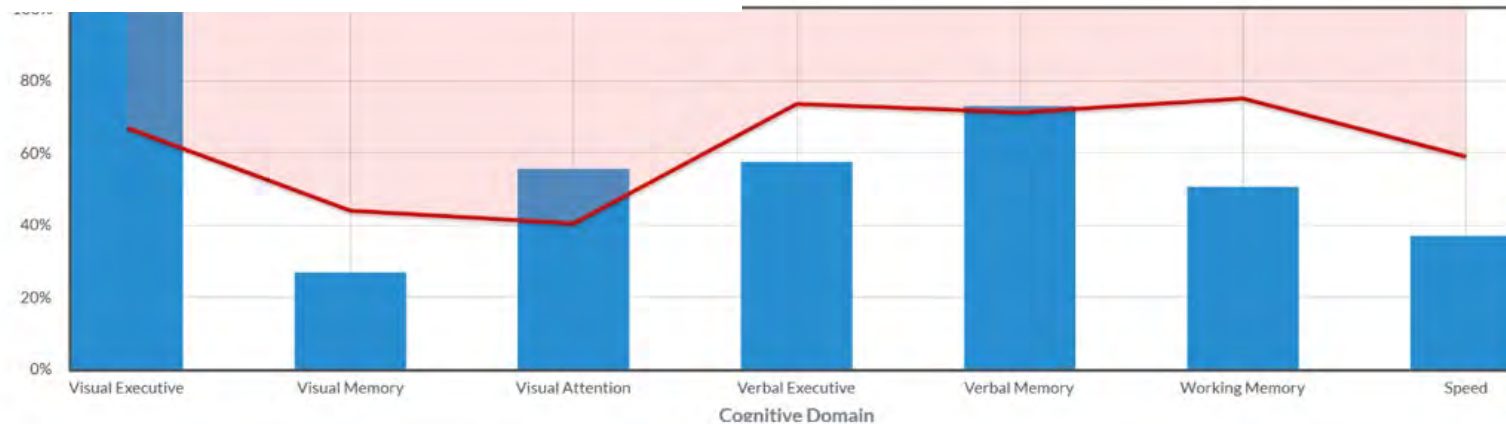

Memobox


Instructions


Help

- Please follow the instructions for this exercise and complete it
- Once complete, you will be prompted to proceed to the next game
- You may resume this activity at a later time (click on this tab's X to close it)

[Click to here to watch the Solitaria introduction video](#)



Graph summarising performance across all training exercises

Peace of Mind

THIS WAY UP ↑↑

Update My DetailsLog

Courses

You are enrolled in the following course(s):

Mixed Depression and Anxiety (Access Expires: 01/08/2018)

People with depression and anxiety experience weeks of sadness, loss of interest and energy, uncontrollable and excessive worry, and avoid situations they feel they can't cope with. This program is designed to help people who experience both depression and anxiety. It involves six lessons over an 8 week period.

Continue CourseView Resources

RegistrationCourse Expiry

63 days remaining

Lesson 1Lesson 2Lesson 3Lesson 4Lesson 5Lesson 6

Mixed Depression and Anxiety

About anxiety and depression

But then, I felt like I wasn't achieving anything, which just made me feel worse...



In this lesson, you will be introduced to Liz and Rob who struggle with depression and anxiety. Here they both learn about their symptoms, and learn how to start tackling the physical symptoms of depression and anxiety.

This course consist of six lessons over an eight week period.

Start Lesson

CHeBA
Healthy Brains • Positive Ageing

 **UNSW**
SYDNEY

Information

 MEDICAL EVENT  HELP  NEWSLETTERS  TICKETS  NOTIFICATIONS 

 Dashboard » MYB Test

 My To-Do List

 Incomplete

Cognitive Training 1

External link containing information about Cognitive Training 1.



Do Activity

I Ne

ALCOHOL AND THE BRAIN

Drinking frequently
memory and thinki
leading to lower br
injuries (e.g. falls or
and other thinking

1. No more than
health problems
2. Do not consum
the risk of alco

The following is an
from the Australia
the label of the co

Number of S



YOUR BRAIN WHEN EXERCISING

Reduce amyloid and tau changes that
are commonly associated with

Alzheimer's disease

Brain-derived neurotrophic
factor (BDNF) is released,
which is important for
maintaining and
repairing

nerve cells

Improve memory,
attention and
processing speed

Reduce vulnerability to
**stress, anxiety
and depression**

Preserve white
matter integrity in
the brain that is
related to **motor
control** and
coordination in
older adults

Increase **blood
flow** to the brain

Increase

- Almost 100,000 participants 55-77yo from 45 and Up study contacted → about 12,000 responded
- 6236 participants randomised – coaching or information
- Up to four modules depending on risk factors
- First year will finish in October 2019
- Boosters monthly for years 2 & 3
- If successful → less cognitive decline by Yr 3
- If more funding ... less dementia by Yr 8
- ... interaction with genetic markers

Drug studies

- Vaccines or enzyme inhibitors against A β
 - A4 Study
 - DIAN – TU
 - Alzheimer Prevention Initiative (Colombia)

Policy Implications

- Australia and the world is ageing
- 30 years of drug trials have failed to find a cure for Alzheimer's disease
- How will Australia cope with
 - ... 430,000 people with dementia now and 1 million within 40 years?
 - ... \$14b+ or 1%GDP → 2% GDP
- Prevention or delay onset critical

Policy Implications

- Can we prevent Alzheimer's and other dementias
- Not yet, but delay onset is possible
- 2- year delay → 20% reduction in prevalence
- 5-year delay → 50% reduction

Ideally delay till after

....

Policy Implications

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- Not yet, but delay onset is possible
- 2- year delay → 20% reduction in prevalence
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Ideally delay till after

.... we die

BE THE CHANGE!

- **Population approach over whole of life**
 - **embryo/childhood may be most important**
 - **Especially education**
 - **Physical activity throughout life**
 - **never too early/ never too late**
 - **Healthy diet – plant based**
 - **Blood pressure control**
- **Health service approach**
 - **Prevention as primary care responsibility**
 - **Everyone's responsibility**



the dementia
momentum[®]

Invest in social
change and help
advance CHeBA's
large-scale, 'big data'
research.

**BECOME A MEMBER
OR FRIEND:**
bit.ly/thedementiamomentum



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www.cheba.unsw.edu.au



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